The observed changes in the expression levels of the studied genes indicate their potential role in tumor progression and a possible impact on their expression of the mutant product of the BRAF gene. Integrins and their ligands, OPN and TSP1, could be considered potential markers in determining the prognosis and treatment of PTC.

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P82a

Molecular biomarkers in preoperative diagnosis of thyroid cancer

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Preoperative differential diagnosis of benign thyroid nodules and thyroid cancer is an important issue of endocrinology. Preoperative identification of a tumor type allows a surgeon to determine an adequate surgical treatment and reduce complications. The cytological analysis of samples obtained by the fine-needle aspiration biopsy is limited in sensitivity and specificity and the core biopsy is not safe to be used in patients with thyroid nodes smaller than 2 cm. The most promising area in the preoperative diagnosis of malignant tumors is molecular biomarkers, which can be used to determine the surgical treatment and indications for the target therapy. BRAF V600E is the most frequent genetic alteration in thyroid cancer. It activates the MAP-kinase pathway which causes changes in expression levels of extracellular matrix proteins and some of their receptors. Changes in the expression of integrin receptors and their ligands, such as osteopontin and thrombospondin-1, contribute to tumor cell proliferation and migration. The C-Jun pathway is also very important in pathogenesis of thyroid cancer. Changes in its activity can affect the expression of GSTP enzyme which participates in hormone metabolism. Altered MiRNA expression has been observed in a variety of cancer states allowing their potential use as cancer biomarkers.

The aim of this study was to evaluate integrins, angiogenic factors, GSTP and MiRNAs as potential biomarkers for the diagnosis and prognosis of thyroid cancer.

112 samples of papillary thyroid cancer (PTC) and 120 samples of benign nodular neoplasms were analyzed. The expression levels of the studied genes were determined by RT-PCR. The results were confirmed by immunohistochemical analysis. The BRAF V600E mutation was determined by allele-specific real-time PCR. The results showed that GSTP can be used for clinical settings as a cancer-specific marker for thyroid neoplasms with 83–88% sensitivity, 70–80% specificity and 76–84% diagnostic accuracy. Higher expression levels of integrins $\alpha 2$, $\alpha 5$, αv, $\alpha 9$, $\beta 1$, $\beta 3$ and IL-8, angiogenin, and VEGF were observed in malignant tumors in comparison with the normal thyroid tissue ($p < 0.05$). The BRAF V600E mutation was detected in 70% of all PTC cases. In the BRAF V600E positive PTC samples the levels of ITGA3 and ITGAV expression were higher than in the BRAF V600E negative ones ($p < 0.05$). The expression of miRNA 21, 221, 222, 155 was significantly increased in the cancer samples compared to the benign neoplasms. Thus, the studied molecular markers could be used for preoperative diagnosis of thyroid neoplasms and the treatment approach.

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A60

The role of metabolic acidosis of peritumoral zone of tumor in enhanced efficiency of antitumor cytostatics

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Background: Metabolic acidosis is a feature of many extreme physiological and pathological conditions; it is characterized by mitochondria dysfunction, increased membrane permeability and changes in the conformation of the protein molecules in violation of their enzymatic properties. In acidosis, intracellular pH shifts to the acidic side, which gives antitumor effect to the cytostatic agent the tumor was resistant to. It is known that the peritumoral zone is a buffer between the tumor and healthy tissue, so abnormalities in the tumor microenvironment changing conditions in peritumoral area will likely affect the tumor status and its response to antitumor therapy. The degree of tissue metabolic acidosis in affected area can be increased by blocking the activity of mitochondria and their contribution to the energy supply of the cells and using pharmacological agents that cause separation of processes of cellular respiration and oxidative phosphorylation. Thus, the conditions of energy blockade can be created in the perifocal area of the tumor. The aim was to study the possibility of increasing the influence of antitumor cytostatic by modeling damages of the energy forming processes in the peritumoral area of the tumor through the creation of metabolic acidosis.

Material and methods: Experimental work fragment was carried out in 60 rats with sarcoma 45 (S45) transplanted under the back skin. Cyclophosphamide (C) was administered intraperitoneally twice at a dose of 5 mg/kg. On the tumor peritumoral area perimeter (in 4 points) 0.25 ml of a 1% solution of ATP or 1% solution of diphenhydramine (D) were administered. Clinical studies were performed on 60 patients diagnosed with breast cancer. These patients underwent two cycles of CMFA chemotherapy: C 800 mg/m^2, methotrexate 30 mg/m^2, fluorouracil 2000 mg/m^2, doxorubicin 80 mg/m[b]; on a background of peritumoral injection of 0.5 ml of a 1% solution of ATP or 1% solution of D.

Results: Modelling of metabolic acidosis in peritumoral area was shown to result in dissociation of respiration processes and oxidative phosphorylation of cells (suppression of SDH activity by ATP by 62% and D by 57.9% and an increase in activity of αGFDG by ATP and D by 154.7%) the ratio of SDH and αGFDG less than 1. Morphologic study of S45 showed the development of wide connective border in the subcapsular zone with the inclusion of